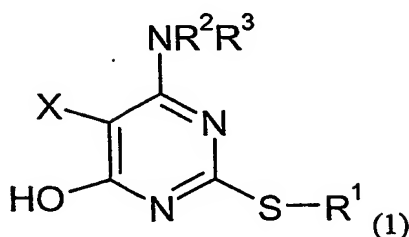


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CLAIMS

1. A compound of formula (1), a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof:



- wherein R¹ is a group selected from C₃₋₇carbocyclyl, C₁₋₈alkyl, C₂₋₆alkenyl and C₂₋₆alkynyl; wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from fluoro, nitrile, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹, phenyl or heteroaryl; wherein phenyl and heteroaryl are optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹, C₁₋₆alkyl and trifluoromethyl;
- wherein R² is C₃₋₇carbocyclyl, optionally substituted by 1, 2 or 3 substituents independently selected from:
- 15 (a) fluoro, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹;
- (b) a 3-8 membered ring optionally containing 1, 2 or 3 atoms selected from O, S, -NR⁸ and whereby the ring is optionally substituted by C₁₋₃alkyl or fluoro; or
- 20 (c) phenyl or heteroaryl, each of which is optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -NR⁸COR⁹, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹, C₁₋₆alkyl and trifluoromethyl;
- or R² is a group selected from C₁₋₈alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl wherein the group is substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C₁₋₆alkoxy, C₁₋₆alkylamino, di(C₁₋₆alkyl)amino, *N*-(C₁₋₆alkyl)-*N*-(phenyl)amino, *N*-C₁₋₆alkylcarbamoyl, *N,N*-(C₁₋₆alkyl)₂carbamoyl, *N*-(C₁₋₆alkyl)-*N*-(phenyl)carbamoyl, carboxy, phenoxycarbonyl, -NR⁸COR⁹, -SO₂R¹⁰, -SO₂NR⁵R⁶ and -NR⁸SO₂R⁹;
- wherein R³ is hydrogen or R²;

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R⁴ is hydrogen or a group selected from C₁₋₆alkyl and phenyl, wherein the group is optionally substituted by 1 or 2 substituents independently selected from halo, phenyl, -OR¹¹ and -NR¹²R¹³;

R⁵ and R⁶ are independently hydrogen or a group selected from C₁₋₆alkyl and phenyl wherein
 5 the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, -OR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶ and NR¹⁵SO₂R¹⁶
 or

R⁵ and R⁶ together with the nitrogen atom to which they are attached form a 4- to
 7-membered saturated heterocyclic ring system optionally containing a further heteroatom
 10 selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by 1, 2 or 3 substituents independently selected from phenyl, -OR¹⁴, -COOR¹⁴, -NR¹⁵R¹⁶, -CONR¹⁵R¹⁶, -NR¹⁵COR¹⁶, -SONR¹⁵R¹⁶, NR¹⁵SO₂R¹⁶ or C₁₋₆alkyl (optionally substituted by 1 or 2 substituents independently selected from halo, -NR¹⁵R¹⁶ and -OR¹⁷ groups);

R¹⁰ is hydrogen or a group selected from C₁₋₆alkyl or phenyl, wherein the group is optionally
 15 substituted by 1, 2 or 3 substituents independently selected from halo, phenyl, -OR¹⁷ and -NR¹⁵R¹⁶; and

each of R⁷, R⁸, R⁹, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷ is independently hydrogen, C₁₋₆alkyl or phenyl;

X is hydrogen, halo, cyano, nitro, hydroxy, C₁₋₆alkoxy (optionally substituted by 1 or 2
 20 substituents selected from halo, -OR¹¹ and -NR¹²R¹³), -NR⁵R⁶, -COOR⁷, -CONR⁵R⁶, -NR⁸COR⁹, thio, thiocyno, thioC₁₋₆alkyl (optionally substituted by 1 or 2 substituents selected from halo, -OR¹⁷, -COOR⁷, -NR¹⁵R¹⁶, -CONR⁵R⁶), -SO₂R¹⁰, -SO₂NR⁵R⁶ -NR⁸SO₂R¹⁰ or a group selected from C₃₋₇carbocyclyl, C₁₋₈alkyl, C₂₋₆alkenyl or C₂₋₆alkynyl, wherein the group is optionally substituted by 1, 2 or 3 substituents independently selected from halo, -OR⁴, -
 25 NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶ and -NR⁸SO₂R⁹; or a phenyl, -heteroaryl, -thiophenyl, -thioheteroaryl, aminoheteroaryl, and thioC₁₋₆alkylheteroaryl group, all of which may be optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹, C₁₋₆alkyl, phenyl, heteroaryl or trifluoromethyl groups;

30

2. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein R¹ is C₁₋₈alkyl optionally substituted by 1, 2 or 3 substituents independently selected from phenyl or heteroaryl, wherein phenyl and heteroaryl

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are optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, -OR⁴, -SR¹⁰, C₁₋₆alkyl and trifluoromethyl.

3. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein R² is C₁₋₈alkyl substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C₁₋₆alkoxy, C₁₋₆alkylamino, di(C₁₋₆alkyl)amino, N-(C₁₋₆alkyl)-N-(phenyl)amino, N-C₁₋₆alkylcarbamoyl, N,N-di(C₁₋₆alkyl)carbamoyl, N-(C₁₋₆alkyl)-N-(phenyl)carbamoyl, carboxy, phenoxycarbonyl, -NR⁸COR⁹, -SO₂R¹⁰, -SO₂NR⁵R⁶ and -NR⁸SO₂R⁹; and wherein R³ is hydrogen;
4. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein R⁴, R⁵, R⁶, R⁸, R⁹ and R¹⁰ are independently hydrogen, C₁₋₄alkyl or phenyl.
5. A compound according to claim 1 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein X is hydrogen, halo, cyano, nitro, hydroxy, thio, thiocyno, -CONR⁵R⁶, thioC₁₋₆alkyl (optionally substituted by 1 or 2 substituents selected from halo, -OR¹⁷, -NR¹⁵R¹⁶, -CONR⁵R⁶), -NR⁸SO₂R¹⁰, C₁₋₈alkyl (optionally substituted by 1, 2 or 3 substituents independently selected from halo, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶ and -NR⁸SO₂R⁹), heteroaryl, thioheteroaryl or thioC₁₋₆alkylheteroaryl all of which may be optionally substituted by 1, 2 or 3 substituents independently selected from halo, cyano, nitro, -OR⁴, -NR⁵R⁶, -CONR⁵R⁶, -COOR⁷, -NR⁸COR⁹, -SR¹⁰, -SO₂R¹⁰, -SO₂NR⁵R⁶, -NR⁸SO₂R⁹, C₁₋₆alkyl or trifluoromethyl.
6. A compound according to claim 2 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein R¹ is benzyl optionally substituted by 1 or 2 substituents independently selected from fluoro, chloro, bromo, methoxy, methyl and trifluoromethyl
7. A compound according to claim 3 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein R² is C₁₋₄alkyl, substituted by 1, 2 or 3 substituents independently selected from hydroxy, amino, C₁₋₆alkoxy, C₁₋₆alkylamino, and di(C₁₋₆alkyl)amino; and R³ is hydrogen;

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8. A compound according to claim 4 or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, wherein X is hydrogen, fluoro, chloro, bromo, thiocyno, -NR⁸SO₂R⁹ (where R⁸ is hydrogen and R⁹ is methyl) -thioimidazolyl, -thiotriazolyl, -CONH₂, -CONMe₂ or cyano.
- 5
9. A compound selected from the group consisting of:
- 2-(Benzylthio)-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 2-(Benzylthio)-5-chloro-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 2-[(3-Chlorobenzyl)thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 10 5-Chloro-2-[(3-chlorobenzyl)thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 2-[(3-Chlorobenzyl)thio]-4-hydroxy-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-pyrimidinyl thiocyanate,
 N-(2-[(3-Chlorobenzyl)thio]-4-hydroxy-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-pyrimidinyl)methanesulfonamide,
 15 2-[(3-Chlorobenzyl)thio]-5-fluoro-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 2-[(2,3-difluorobenzyl)thio]-4-hydroxy-6-{[(1S)-2-hydroxy-1-methylethyl]amino}pyrimidine-5-carbonitrile,
 5-Chloro-2-[(2,3-difluorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 20 2-[(2,3-Difluorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-iodo-4-pyrimidinol,
 2-[(2,3-Difluorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-nitro-4-pyrimidinol,
 2-[(3-Chlorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-(1,3,4-thiadiazol-2-ylthio)-4-pyrimidinol,
 25 2-[(2,3-Difluorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-(1H-imidazol-2-ylthio)-4-pyrimidinol,
 2-[(2,3-Difluorophenyl)methyl]thio]-5-[[2-(dimethylamino)ethyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-pyrimidinol,
 30 1-[2-[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-pyrimidinyl]-4(1H)-pyridinethione,
 2-[(2,3-Difluorophenyl)methyl]thio]-6-{[(1R)-2-hydroxy-1-methylethyl]amino}-5-(4-pyridinylthio)-4-pyrimidinol,

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- 2-[[[(2,3-Difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-(1*H*-1,2,4-triazol-3-ylthio)-4-pyrimidinol,
- 2-[[[(2,3-Difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(4-methyl-4*H*-1,2,4-triazol-3-yl)thio]-4-pyrimidinol,
- 5 5-[(5-Amino-4*H*-1,2,4-triazol-3-yl)thio]-2-[[[(2,3-difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-4-pyrimidinol,
- 2-[[[(2,3-Difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(5-(4-pyridinyl)-1,3,4-oxadiazol-2-yl)thio]-4-pyrimidinol,
- Ethyl[[2-[[[(2,3-difluorophenyl)methyl]thio]-4-hydroxy-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]-AcOH,
- 10 2-[[2-[[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]-*N*-methyl- acetamide,
- 2-[[2-[[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]-*N*-[2-(dimethylamino)ethyl]- acetamide,
- 15 1-[[2-[[[(2,3-Difluorophenyl)methyl]thio]-4-hydroxy-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-pyrimidinyl]thio]acetyl]-piperazine,
- 2-[[[(2,3-Difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(4-methyl-2-oxazolyl)thio]-4-pyrimidinol,
- 2-[[[(2,3-Difluorophenyl)methyl]thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(1,2,4-oxadiazol-3-ylmethyl)thio]-4-pyrimidinol,
- 20 2-[(2,3-difluorobenzyl)thio]-4-[[[(1*R*)-1,2-dihydroxyethyl]amino]-6-hydroxypyrimidine-5-carboxamide,
- 2-[(2,3-difluorobenzyl)thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-(5-methyl-1,2,4-oxadiazol-3-yl)pyrimidin-4-ol,
- 25 2-[(2,3-difluorobenzyl)thio]-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-(1,3-oxazol-5-yl)pyrimidin-4-ol,
- 2-[(2,3-difluorobenzyl)thio]-4-[[[(1*R*)-1,2-dihydroxyethyl]amino]-6-hydroxy-*N,N*-dimethylpyrimidine-5-carboxamide,
- 2-[(2,3-difluorobenzyl)thio]-5-fluoro-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-pyrimidin-4-
- 30 ol,
- 2-[(3,4-difluorobenzyl)thio]-5-fluoro-6-[[[(1*R*)-2-hydroxy-1-methylethyl]amino]-pyrimidin-4-ol,

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2-[(3-fluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}pyrimidin-4-ol,
or
2-[(4-fluorobenzyl)thio]-5-fluoro-6-{[(1*R*)-2-hydroxy-1-methylethyl]amino}pyrimidin-4-ol
and a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof.

5

10. A compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament.

11. A compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester
10 thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

12. A compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester
15 thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of cancer.

13. A compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 9 for use as a medicament for the treatment of
20 COPD.

14. The use of a compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of human diseases or conditions in which modulation of
25 chemokine receptor activity is beneficial.

15. The use of a compound, pharmaceutically acceptable salt, solvate, or *in vivo* hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel
30 disease, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.

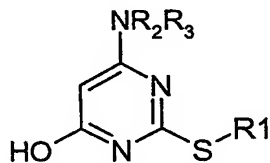
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16. The use of a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of cancer

17. A pharmaceutical composition comprising a compound, pharmaceutically acceptable salt, solvate, or in vivo hydrolysable ester thereof according to any one of claims 1 to 9; and a pharmaceutically-acceptable diluent or carrier.

18. A process for the preparation of a compound of formula (1) as defined above which comprises

(a) treating a compound of formula (2):



(2)

wherein R^1 , R^2 and R^3 are as defined in formula (1), with suitable electrophiles.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups;

ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

(iv) forming a prodrug

(v) forming an in vivo hydrolysable ester; or

(b), where X is 1,3-oxazol-5-yl by treating a compound of formula (4):



(4)

25

wherein R^1 , R^2 and R^3 are as defined in formula (1), X is $-CHO$ and Y is protected hydroxy by treatment with *p*-toluenesulfonylmethyl isocyanide and potassium hydroxide in refluxing methanol.

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and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

i) removing any protecting groups;

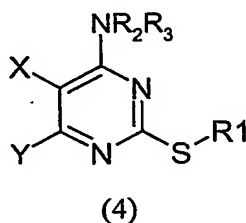
ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

5 (iv) forming a prodrug,

v) forming an *in vivo* hydrolysable ester; or

(c) where X is CN by treating a compound of formula (4):



10

wherein R^1 , R^2 and R^3 are as defined in formula (1), X is CN and Y is halogen by treatment with potassium *tert*-butoxide in refluxing aqueous toluene.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

15 i) removing any protecting groups,

ii) converting the compound of formula (1) into a further compound of formula (1),

iii) forming a salt;

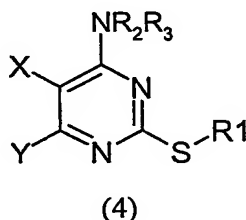
(iv) forming a prodrug,

v) forming an *in vivo* hydrolysable ester; or

20

(d) where X is $-\text{CONR}^5\text{R}^6$ by;

c) treating a compound of formula (4):



25

wherein R^1 , R^2 and R^3 are as defined in formula (1), X is $-\text{CONR}^5\text{R}^6$ and Y is halogen with a suitable base.

and optionally thereafter (i), (ii), (iii), (iv) or (v) in any order:

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- i) removing any protecting groups;
 - ii) converting the compound of formula (1) into a further compound of formula (1),
 - iii) forming a salt;
 - (iv) forming a prodrug,
 - 5 v) forming an *in vivo* hydrolysable ester.
19. A combination therapy which comprises administering a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, or a pharmaceutical composition or formulation comprising a compound of formula (1),
- 10 concurrently or sequentially with other therapy and/or another pharmaceutical agent.
20. A combination therapy as claimed in claim 19 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.
- 15
21. A combination therapy as claimed in claim 19 for the treatment of cancer.
22. A pharmaceutical composition which comprises a compound of formula (1) or a pharmaceutically acceptable salt, solvate or *in vivo* hydrolysable ester thereof, in conjunction
- 20 with another pharmaceutical agent.
23. A pharmaceutical composition as claimed in claim 22 for the treatment of asthma, allergic rhinitis, COPD, inflammatory bowel disease, irritable bowel syndrome, osteoarthritis, osteoporosis, rheumatoid arthritis, or psoriasis.
- 25
24. A pharmaceutical composition as claimed in claim 22 for the treatment of cancer.